International Academy
of Compounding Pharmacists

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Dockets Management Branch
Food and Drug Administration
(HFA-305), Room 1061
5630 Fishers Lane
Rockville, Maryland 20852

Re: Docket Number 98N-1265
Federal/State Memorandum of Understanding On Interstate Distribution of Compounded Drug Products

Dear Sir or Madam:

The following comments are submitted by the International Academy of Compounding Pharmacists (IACP) in response to the Food and Drug Administration's (FDA's) request for comments on its draft Federal/State Memorandum of Understanding on Interstate Distribution of Compounded Drug Products. 64 Fed. Reg. 3301 (Jan. 21, 1999). IACP is an international organization of compounding pharmacists.

As a preliminary matter, IACP requests that FDA withdraw the draft MOU as published because the agency has failed to comply with the procedural requirement for consultation with the National Association of Boards of Pharmacy (NAPB). IACP has been advised that NAPB did not have an opportunity to provide substantive consultation to the FDA on development of the MOU. Rather, we have been informed that FDA simply provided a copy of the MOU to NABP, but did not consult with that group or wait for feedback from NABP before publishing this draft. FDA's failure to involve the NAPB is any meaningful way violates the nondelegation doctrine. American Trucking Association, Inc. v. EPA, No. 97-1440 (D.C. Cir. May 14, 1999). See also, J.W.

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Hampton, Jr. & Co. v. United States Congress, 276 U.S. 394 (1928). In specifically requiring consultation with NAPB, Congress expected FDA to utilize that consultation to "articulate an intelligible principle," establishing the proper role of the states in investigating complaints and in establishing what constitutes compounding in "inordinate amounts." The result is that FDA has developed an MOU that lacks the knowledge and understanding of pharmacy compounding at the state level, that Congress expected the agency to obtain.

Because consultation with NAPB is a statutory requirement, section 503A(b)(3)(B), the MOU must be withdrawn from further consideration until that consultation is obtained. FDA may republish the MOU with a new period for notice and comment only after it has consulted with NABP.

The draft MOU addresses the key points Congress intended for inclusion in the MOU. However, FDA has misinterpreted the statute with respect to the types of complaints that states must investigate and, as a result, imposes significant burdens on state boards of pharmacy. This section should be revised to reflect Congress' intent. In addition, IACP opposes the imposition of any limitation on the percentage of compounded prescriptions that may be shipped interstate. The decision that a compounded prescription is needed is entrusted to physicians and accomplished only through the pharmacist-patient-practitioner triad. Arbitrary "ceilings" on the amount of prescriptions that may be compounded is unnecessarily disruptive to the practice of medicine and can only jeopardize the quality of patient care.

The MOU Imposes Inappropriate Burdens on the State Boards

The nature and extent of complaint investigation required in the MOU exceeds the authority vested in state boards of pharmacy by the states. The compounding provision of the Food and Drug Administration Modernization Act (FDAMA) states that the MOU between FDA and the states must provide "for appropriate investigation by a state agency of complaints relating to compounded drug products distributed outside such state." 21 U.S.C. § 503A(b)(3)(B)(i). However, this does not entitle FDA to compel states to investigate complaints of all types. There is nothing in the legislative history of the compounding provision that supports such a massive transfer of responsibilities to the states.

During the legislative process, FDA expressed concerns over the possibility that out-of-state injuries may not be properly investigated. Product-related complaints as defined by FDA regulations include complaints concerning serious and unexpected adverse events and complaints involving the possible failure of a drug to meet any of its specifications. See 21 C.F.R. § 211.198. These are the "complaints" Congress contemplated would be subject to this provision. Congress did not expect states to be surrogate FDAs with responsibility for enforcing all the limitations set out in section 503A. Moreover, IACP believes that states are investigating product-related complaints.

The other types of complaints set forth in the draft MOU, such as ensuring that compounding pharmacies use only bulk drugs manufactured in FDA-approved facilities or that all drugs are accompanied by a certificate of analysis, have no place in this document. These "complaints" simply should not be the responsibility of the states.

The MOU should not compel the states to act as an investigative arm whenever anyone who dislikes a compounding pharmacy complains about an interstate shipment. Thrusting that role on the state boards goes beyond the intent of FDAMA and is a misguided effort to micromanage state boards. State boards must use their resources in a manner that will protect the well-being of patients, and in a manner consistent with state law. Investigating complaints that compounded drugs shipped out of state were made with drugs not covered by FDAMA provisions is a task that FDA cannot assign to the states. It is inappropriate, and burdensome, to ask states to handle these complaints simply because the complaint arose from a drug that crossed state lines. It is equally inappropriate to insist that state boards maintain records that are irrelevant to the tasks that it was empowered to do by the state. In trying to use the MOU to require state boards to investigate activities that are outside the scope of their mandate, FDA has forgotten that the responsibility for the state boards is determined by state law, not section 503A of FDAMA.

Moreover, FDA's proposals for coordination with the states are overly prescriptive. FDA states that "[t]he standard MOU reflects FDA's policy to *defer* to State and local officials for the regulation of the day-to-day practice of pharmacy"[1] (emphasis added). However, the MOU takes the form of an unfunded mandate by literally dictating the way in which complaints about adverse events, alleged violations of the compounding provision, and other alleged violations are to be handled. In doing so, FDA requires the availability of state staff, resources and facilities by state boards. Although the Unfunded Mandate Law (2 U.S.C. § 1501 et. seq.) anticipates that "mandates" from government agencies would take the form of proposed rulemakings, the MOU has the same effect and FDA should not be excused from examining the economic impact on states simply because the mandate takes the form of an MOU. Therefore, before the MOU is finalized, FDA must take the steps as directed under section 1532 of the Unfunded Mandate Law to assess the costs and benefits associated with implementation of the MOU, and state whether federal funding will be made available to the states for the purposes of complying with the MOU. FDA has described no efforts to assess the costs this mandate will impose upon the states. FDA must undertake this type of analysis before causing the states to incur these costs.

1 FDA, Memorandum of Understanding on Interstate Distribution of Compounded Drug Products between the [State Agency] and the U.S. Food and Drug Administration, 4 (Dec. 23, 1998).

The MOU Imposes Inappropriate Restrictions on the Interstate Distribution of Compounded Drugs

IACP also objects to FDA's proposals to impose "ceilings" on the interstate shipment of compounded drugs. FDA says that for the purposes of the MOU, interstate distribution of an "inordinate amount of compounded drugs" occurs if the number of compounded prescriptions distributed interstate on an annual basis is equal to or greater than 20% of the total number of prescriptions dispensed or distributed by that pharmacy (including both intrastate and interstate prescriptions), or if prescriptions for one or more individual compounded drug products (including varying strengths of the same active ingredient) constitute more than 5% of the total number of prescriptions dispensed or distributed by the pharmacy. This would interfere with the practice of medicine by restricting physician prescription practices, as only a limited percentage of patients could receive compounded prescriptions.

Nothing in section 503A or the legislative history suggests that Congress intended that FDA should impose a specific ceiling on the amount of compounded drugs that could be shipped interstate under the MOU. If Congress believed that the imposition of a standard ceiling was an appropriate resolution, it could have included that ceiling in the text of 503A. But Congress did not take that approach. FDA provides no rationale for the imposition of inflexible ceilings. While Congress set 5% as a default ceiling, this does not imply that a ceiling is required at all, because Congress made no finding that the shipment of any percentage was "inordinate." FDA should determine that even the shipment of 100% of compounded drugs out of state is not "inordinate," provided that all of the other requirements in 503A are met. Moreover, the specific ceilings selected by FDA are arbitrary and unconstitutional, bearing no rational relationship to the practice of medicine or pharmacy, or to the needs of patients.

The most serious concern is that ceilings will have an adverse effect on the quality of patient care. Some pharmacies specialize in pharmacy compounding. As a result, the experience of those pharmacies in compounding safe and reliable products draws prescriptions from physicians in other states. By arbitrarily limiting the interstate distribution of compounded drugs, FDA will force pharmacies to ration their out-of-state shipments. How should a small pharmacy that has a unique ability to compound a product decide which few out-of-state patients should receive the therapy prescribed by their physician? As drafted, the MOU will force patients to get their prescriptions filled from pharmacies based on their location and not based on their relationship with the pharmacist, or the pharmacist's experience in compounding the specific prescription.

Furthermore, the 5% limit imposed on individual products fails to recognize that those orders exist precisely because there is no commercially available product to meet patient needs. This includes drugs compounded for patients with AIDS and specific types of cancer, such as malignant melanoma.

Moreover, the ceilings and FDA's proposal to allow pharmacies to exclude prescriptions dispensed within a 50-mile radius from the ceiling calculations are unconstitutional. The ceilings and the exclusion calculation are violative of the Fifth Amendment because they result in disparate treatment of pharmacies based solely on their geographic location. The federal government violates the due process clause of the Fifth Amendment when it makes a classification which, if it were made by a state, would violate the Fourteenth Amendment's Equal Protection clause. Bolling v. Sharp, 347 U.S. 497 (1954). Moreover, the federal government cannot force the states to take such action. As the Supreme Court reiterated in a recent decision, Congress cannot "enlist state cooperation in a joint federal-state program by legislation which authorizes the States to violate the Equal Protection Clause." Saenz v. Roe, 1999 U.S. Lexis 3174 (U.S. May 17, 1999), at Footnote 21, quoting Shapiro v. Thompson, 394 U.S. 618, 641 (1969).

First, pharmacies located near state borders are likely to have disproportionately larger percentages of prescriptions that enter interstate commerce. As a result, the ceilings will have a greater economic impact on those pharmacies. Moreover, FDA's 50-mile exclusion, no matter how well intentioned, serves only to exacerbate the disparate impact of the MOU on pharmacies. Pharmacies located in coastal areas, such as Rhode Island, could lose as much as 50% of the intended benefit of the exclusion calculation if half of the 50-mile radius includes coastal waters. Pharmacies located in geographically remote areas, such as Hawaii and Alaska, will lose 100% of the benefit simply because there are no states within a 50-mile radius. Pharmacies located 51 miles from the border will not benefit from the 50-mile exclusion at all, while pharmacies on the border will be able to exclude a shipping area of up to roughly 4,000 square miles.

More fundamentally, the idea that limits on interstate shipments are necessary to protect patients or prevent "manufacturing in the guise of compounding" is untenable. The passage of compounded drugs across state borders affects neither patient care nor determines whether a pharmacy is acting as a "manufacturer." The act of crossing a state line does not transform a compounded drug into a manufactured drug.

While the Supreme Court accords great deference in the application of classifications that result from economic legislation, the classification must bear some rational relationship to a legitimate legislative objective. Lindsley v. National Carbonic Gas Co., 220 U.S. 61 (1911). FDA's proposed ceilings fail this test because the government has not demonstrated any rational basis for establishing that standard ceilings, including the specific ceilings selected, represent "inordinate amounts of compounded drugs" based on the practice of medicine or pharmacy. And, FDA certainly cannot show that the caps serve the objective of providing quality patient care.

Congress's goal in including the option of the MOU was to encourage states to work with the FDA. The legislative alternative is acceptance of the 5% cap on interstate distribution provided in section 503A which severely limits the options available to patients and pharmacists. A state that declines to enter into the MOU puts its pharmacists at a severe handicap.

In her statement to the Pharmacy Compounding Advisory Committee in October of 1998, before the proposed MOU was drafted, Kate Lambrew Hull, Legislative Assistant to Senator Tim Hutchinson, one of the architects of the compounding provision, noted that the inclusion of the restrictive 5% limit was a key issue "because we really want states to enter into this MOU."[2] Thus, while entering into the MOU is voluntary, the alternative was designed to be so confining as to virtually compel the states to enter the MOU. It is inappropriate for FDA to use the leverage provided by Congress to coerce states to enter into an MOU that fails to serve the needs of patients, forces the states to take on tasks that are not theirs, and interferes with existing state laws and states' rights.

FDA must discard the MOU in its current form and consult NABP. The MOU is flawed in theory and design. IACP and its members are prepared to assist the FDA in developing an appropriate MOU that ensures that patients' interests are served and Congress' objectives furthered.

Sincerely,

Gina Ford, R.Ph.
Executive Director
International Academy of
Compounding Pharmacists

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2 FDA, Pharmacy Compounding Advisory Committee Meeting, Statement of Kate Lambrew Hull at 15 (Oct. 14, 1998).